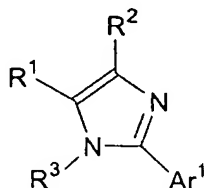


WHAT IS CLAIMED IS:

1. A method of treating a disease mediated by the Cannabinoid-1 receptor comprising administration to a patient in need of such treatment of a therapeutically effective amount of a compound of structural formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

R¹ is selected from:

- (1) hydrogen,
- (2) C₁₋₄alkyl,
- (3) C₂₋₄alkenyl,
- (4) C₂₋₄alkynyl,
- (5) C₃₋₇cycloalkyl,
- (6) C₃₋₇cycloalkyl-C₁₋₄alkyl,
- (7) cycloheteroalkyl,
- (8) cycloheteroalkyl-C₁₋₄alkyl,
- (9) aryl, and
- (10) heteroaryl;

- wherein alkyl, alkenyl, alkynyl, cycloalkyl, and cycloheteroalkyl are optionally substituted with one to four substituents independently selected from R^a, and aryl and heteroaryl are optionally substituted with one to four substituents independently selected from R^b;

R² is selected from:

- (1) -OR^c,
- (2) -OC(O)R^c,
- (3) -OC(O)NR^cR^d,
- (4) -SR^c,
- (5) -S(O)_mR^c,

- 5
- (6) $-\text{SO}_2\text{NR}^c\text{R}^d$,
 - (7) $-\text{NR}^c\text{R}^d$,
 - (8) $-\text{NR}^c\text{C}(\text{O})\text{R}^d$,
 - (9) $-\text{NR}^c\text{SO}_2\text{R}^d$,
 - (10) $-\text{NR}^c\text{C}(\text{O})\text{NR}^c\text{R}^d$,
 - (11) $-\text{NR}^c\text{C}(\text{O})\text{OR}^d$,
 - (12) $-\text{C}(\text{O})\text{OR}^c$, and
 - (13) $-\text{C}(\text{O})\text{NR}^c\text{R}^d$;

R^3 is selected from:

- 10
- (1) $-\text{C}_{1-10}\text{alkyl}$, and
 - (2) $-\text{Ar}^2$;

Ar^1 and Ar^2 are independently selected from phenyl, naphthyl, thienyl, furanyl, pyrrolyl, benzothienyl, benzofuranyl, indanyl, indenyl, indolyl, tetrahydronaphthyl, 2,3-dihydrobenzofuranyl, dihydrobenzopyranyl, and 1,4-benzodioxanyl, each

- 15 optionally substituted with one, two, or three groups independently selected from R^b ; each R^a is independently selected from:

- 20
- (1) $-\text{OR}^c$,
 - (2) $-\text{NR}^c\text{S}(\text{O})_m\text{R}^d$,
 - (3) halogen,
 - (4) $-\text{S}(\text{O})_m\text{R}^c$,
 - (5) $-\text{SR}^c$,
 - (6) $-\text{S}(\text{O})_2\text{OR}^c$,
 - (7) $-\text{S}(\text{O})_m\text{NR}^c\text{R}^d$,
 - (8) $-\text{NR}^c\text{R}^d$,
 - 25 (9) $-\text{O}(\text{CR}^e\text{R}^f)_n\text{NR}^c\text{R}^d$,
 - (10) $-\text{C}(\text{O})\text{R}^c$,
 - (11) $-\text{CO}_2\text{R}^c$,
 - (12) $-\text{CO}_2(\text{CR}^e\text{R}^f)_n\text{CONR}^c\text{R}^d$,
 - (13) $-\text{OC}(\text{O})\text{R}^c$,
 - 30 (14) $-\text{CN}$,
 - (15) $-\text{C}(\text{O})\text{NR}^c\text{R}^d$,
 - (16) $-\text{NR}^c\text{C}(\text{O})\text{R}^d$,
 - (17) $-\text{OC}(\text{O})\text{NR}^c\text{R}^d$,
 - (18) $-\text{NR}^c\text{C}(\text{O})\text{OR}^d$,

- (19) $-\text{NR}^c\text{C}(\text{O})\text{NR}^c\text{R}^d$,
 (20) $-\text{CR}^c(\text{N}-\text{OR}^d)$,
 (21) $-\text{CF}_3$,
 (22) $-\text{OCF}_3$,
 5 (23) C_3 -8cycloalkyl, and
 (24) cycloheteroalkyl;
 each R^b is independently selected from:
- (1) C_1 -6alkyl,
 (2) C_2 -6alkenyl,
 10 (3) C_2 -6alkynyl,
 (4) $-\text{OR}^c$,
 (5) $-\text{NR}^c\text{S}(\text{O})_m\text{R}^d$,
 (6) $-\text{NO}_2$,
 (7) halogen,
 15 (8) $-\text{S}(\text{O})_m\text{R}^c$,
 (9) $-\text{SR}^c$,
 (10) $-\text{S}(\text{O})_2\text{OR}^c$,
 (11) $-\text{S}(\text{O})_m\text{NR}^c\text{R}^d$,
 (12) $-\text{NR}^c\text{R}^d$,
 20 (13) $-\text{O}(\text{CR}^e\text{R}^f)_n\text{NR}^c\text{R}^d$,
 (14) $-\text{C}(\text{O})\text{R}^c$,
 (15) $-\text{CO}_2\text{R}^c$,
 (16) $-\text{CO}_2(\text{CR}^e\text{R}^f)_n\text{CONR}^c\text{R}^d$,
 (17) $-\text{OC}(\text{O})\text{R}^c$,
 25 (18) $-\text{CN}$,
 (19) $-\text{C}(\text{O})\text{NR}^c\text{R}^d$,
 (20) $-\text{NR}^c\text{C}(\text{O})\text{R}^d$,
 (21) $-\text{OC}(\text{O})\text{NR}^c\text{R}^d$,
 (22) $-\text{NR}^c\text{C}(\text{O})\text{OR}^d$,
 30 (23) $-\text{NR}^c\text{C}(\text{O})\text{NR}^c\text{R}^d$,
 (24) $-\text{CR}^c(\text{N}-\text{OR}^d)$,
 (25) $-\text{CF}_3$,
 (26) $-\text{OCF}_3$,
 (27) C_3 -8cycloalkyl,

(28) cycloheteroalkyl, and

(29) phenyl;

each R^c and R^d is independently selected from:

- (1) hydrogen,
- 5 (2) C₁₋₁₀alkyl,
- (3) C₂₋₁₀alkenyl,
- (4) C₂₋₁₀alkynyl,
- (5) -NH(C₁₋₁₀alkyl),
- (6) -N(C₁₋₁₀alkyl)₂,
- 10 (7) cycloalkyl,
- (8) cycloalkyl-C₁₋₁₀alkyl;
- (9) cycloheteroalkyl,
- (10) cycloheteroalkyl-C₁₋₁₀alkyl;
- (11) aryl,
- 15 (12) heteroaryl,
- (13) aryl-C₁₋₁₀alkyl, and
- (14) heteroaryl-C₁₋₁₀alkyl, or

R^c and R^d together with the atom to which they are attached form a heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from

20 oxygen, sulfur and N-R^c,

each R^c and R^d may be unsubstituted or substituted with one to three substituents selected from R^e;

each R^e and R^f is independently selected from:

- (1) hydrogen,
- 25 (2) C₁₋₁₀alkyl,
- (3) C₂₋₁₀alkenyl,
- (4) C₂₋₁₀alkynyl,
- (5) cycloalkyl,
- (6) cycloalkyl-C₁₋₁₀alkyl,
- 30 (7) cycloheteroalkyl,
- (8) cycloheteroalkyl-C₁₋₁₀alkyl,
- (9) aryl,
- (10) heteroaryl,
- (11) aryl-C₁₋₁₀alkyl, and

- (12) heteroaryl-C₁₋₁₀ alkyl, or
R^e and R^f together with the carbon to which they are attached form a ring of 5 to 7
members containing 0-2 heteroatoms independently selected from oxygen, sulfur and
nitrogen;
5 m is selected from 1 and 2; and
n is selected from 1, 2, and 3.

2. The method according to Claim 1 wherein the disease mediated
by the Cannabinoid-1 receptor is selected from: psychosis, memory deficit, cognitive
10 disorders, migraine, neuropathy, neuro-inflammatory disorders, cerebral vascular
accidents, head trauma, anxiety disorders, stress, epilepsy, Parkinson's disease,
schizophrenia, substance abuse disorders, constipation, chronic intestinal pseudo-
obstruction, cirrhosis of the liver, asthma, obesity, and other eating disorders
associated with excessive food intake.

15

3. The method according to Claim 2 wherein the disease mediated
by the Cannabinoid-1 receptor is an eating disorder associated with excessive food
intake.

20

4. The method according to Claim 3 wherein the eating disorder
associated with excessive food intake is selected from obesity, bulimia nervosa, and
compulsive eating disorders.

5. The method according to Claim 4 wherein the eating disorder
25 associated with excessive food intake is obesity.

6. The method according to Claim 1, wherein in the compound of
structural formula I:

R¹ is selected from:

- 30 (1) hydrogen,
(2) C₁₋₄alkyl,
(3) C₂₋₄alkenyl,
(4) C₂₋₄alkynyl,
(5) C₃₋₇cycloalkyl, and

(6) C₃₋₇cycloalkyl-C₁₋₄alkyl,

wherein alkyl, alkenyl, alkynyl, and cycloalkyl, are optionally substituted with one to four substituents independently selected from R^a;

R² is selected from:

- 5 (1) -OR^c,
- (2) -SR^c,
- (3) -S(O)_mR^c,
- (4) -SO₂NR^cR^d,
- (5) -NR^cR^d,
- 10 (6) -NR^cC(O)R^d,
- (7) -NR^cSO₂R^d,
- (8) -C(O)OR^c, and
- (9) -C(O)NR^cR^d;

R³ is selected from:

- 15 (1) - C₁₋₄ alkyl, and
- (2) - Ar²;

Ar¹ and Ar² are independently selected from phenyl, naphthyl, thienyl, each optionally substituted with one or two groups independently selected from R^b;

each R^a is independently selected from:

- 20 (1) -OR^c,
- (2) -NR^cS(O)_mR^d,
- (3) halogen,
- (4) -S(O)_mR^c,
- (5) -SR^c,
- 25 (6) -S(O)_mNR^cR^d,
- (7) -NR^cR^d,
- (8) -O(CR^eR^f)_nNR^cR^d,
- (9) -C(O)R^c,
- (10) -CN,
- 30 (11) -C(O)NR^cR^d,
- (12) -NR^cC(O)R^d,
- (13) -CF₃,
- (14) -OCF₃,
- (15) C₃₋₈cycloalkyl, and

(16) cycloheteroalkyl;

each R^b is independently selected from:

- (1) C₁₋₆alkyl,
- (2) -OR^c,
- 5 (3) halogen,
- (4) -CN,
- (5) -C(O)NR^cR^d,
- (6) -NR^cC(O)R^d,
- (7) CF₃,
- 10 (8) -OCF₃, and
- (9) phenyl;

each R^c and R^d is independently selected from:

- (1) hydrogen,
- (2) -C₁₋₁₀ alkyl,
- 15 (3) -NH(C₁₋₁₀ alkyl),
- (4) -N(C₁₋₁₀ alkyl)₂,
- (5) cycloalkyl, and
- (6) cycloheteroalkyl, or

R^c and R^d together with the atom to which they are attached form a heterocyclic ring
20 of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-R^c,

each R^c and R^d may be unsubstituted or substituted with one to three substituents selected from R^e;

each R^e and R^f is independently selected from:

- 25 (1) hydrogen,
- (2) C₁₋₁₀alkyl,
- (3) cycloheteroalkyl,
- (4) cycloheteroalkyl-C₁₋₁₀ alkyl,
- (5) aryl,
- 30 (6) heteroaryl,
- (7) aryl-C₁₋₁₀ alkyl, and
- (8) heteroaryl-C₁₋₁₀ alkyl, or

R^e and R^f together with the carbon to which they are attached form a ring of 5 to 7 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and nitrogen;
or a pharmaceutically acceptable salt thereof.

5

7. The method according to Claim 6, wherein in the compound of structural formula I:

R¹ is selected from:

- (1) hydrogen, and
10 (2) C₁₋₄ alkyl;

R² is selected from:

- (1) -OR^c,
(2) -NR^cR^d,
(3) -NR^cC(O)R^d,
15 (4) -NR^cSO₂R^d,
(5) -C(O)OR^c, and
(6) -C(O)NR^cR^d;

R³ is selected from:

- (1) - methyl, and
20 (2) - Ar²;

Ar¹ and Ar² are phenyl, each optionally substituted with one or two groups independently selected from R^b;

each R^e and R^f is independently selected from:

- (1) hydrogen,
25 (2) C₁₋₁₀alkyl,
(3) cycloheteroalkyl,
(4) aryl, and
(5) heteroaryl;

or a pharmaceutically acceptable salt thereof.

30

8. The method according to Claim 7, wherein in the compound of structural formula I:

R¹ is selected from:

- (1) hydrogen,
(2) methyl, and

(3) ethyl;

R² is selected from:

- 5 (1) -OR^c,
(2) -NR^cC(O)R^d,
(3) -C(O)OR^c, and
(4) -C(O)NR^cR^d;

Ar¹ and Ar² are each independently selected from:

- 10 (1) phenyl,
(2) 4-fluorophenyl,
(3) 2-chlorophenyl,
(4) 3-chlorophenyl,
(5) 4-chlorophenyl,
(6) 4-cyanophenyl,
(7) 4-methylphenyl,
15 (8) 4-isopropylphenyl,
(9) 4-biphenyl,
(10) 4-bromophenyl,
(11) 4-iodophenyl,
(12) 2,4-dichlorophenyl, and
20 (13) 2-chloro-4-fluorophenyl;

each R^c and R^d is independently selected from:

- (1) hydrogen,
(2) methyl,
(3) ethyl,
25 (4) -N(CH₃)₂,
(5) -NH(CH₃),
(6) cyclopentane,
(7) cyclohexane,
(8) cycloheptane,
30 (9) piperidine,
(10) morpholine,
(11) pyrrolidine,
(12) azepine, and
(13) 4-methylpiperazine,

each R^c and R^d may be unsubstituted or substituted with one to three substituents selected from R^e;
or a pharmaceutically acceptable salt thereof.

- 5 9. The method according to Claim 8, wherein in the compound according to structural formula I:
R¹ is methyl;
R² is -C(O)NR^cR^d;
R³ is -Ar²;
10 Ar¹ is 2,4-dichlorophenyl;
Ar² is 4-chlorophenyl;
each R^c and R^d is independently selected from:
 (1) hydrogen,
 (2) cyclohexane, and
15 (3) piperidine,
each R^c and R^d may be unsubstituted or substituted with one to three substituents selected from R^e;
or a pharmaceutically acceptable salt thereof.

- 20 10. The method according to Claim 1, wherein the compound of structural formula I is selected from:
 (1) ethyl 1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxylate;
 (2) ethyl 2-(2,4-dichlorophenyl)-1,5-dimethyl-imidazole-4-carboxylate;
25 (3) N-(cyclohexyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
 (4) N-(piperidin-1-yl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
 (5) N-(piperidin-1-yl)-2-(2,4-dichlorophenyl)-1,5-dimethyl-imidazole-4-carboxamide;
30 (6) N-(cyclopentyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
 (7) N-(cycloheptyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;

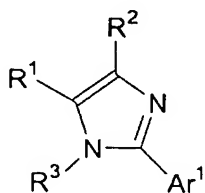
- (8) N-(morpholin-4-yl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (9) N-(pyrrolidin-1-yl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 5 (10) N-(azepin-1-yl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (11) N-(4-methylpiperazin-1-yl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 10 (12) N',N'-dimethyl-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxhydrazide;
- (13) N-(cyclohexyl)-1-(phenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (14) N-(piperidin-1-yl)-1-(phenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 15 (15) N-(cyclohexyl)-1-(4-fluorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (16) N-(piperidin-1-yl)-1-(4-fluorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (17) N-(4-methyl-cyclohexyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide (Isomer A);
- 20 (18) N-(2-(pyrrolidin-1-yl)ethyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (19) N-(cyclohexyl)-1-(4-chlorophenyl)-2-(2-chlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 25 (20) N-(piperidin-1-yl)-1-(4-chlorophenyl)-2-(2-chlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (21) N-(cyclohexyl)-1-(4-bromophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 30 (22) N-(piperidin-1-yl)-1-(4-bromophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (23) N-(cyclohexyl)-1-(4-isopropylphenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (24) N-(piperidin-1-yl)-1-(4-isopropylphenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;

- (25) N-(cyclohexyl)-1-(4-cyanophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (26) N-(piperidin-1-yl)-1-(4-cyanophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 5 (27) N-(cyclohexyl)-1-(4-biphenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (28) N-(piperidin-1-yl)-1-(4-biphenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (29) N-(cyclohexyl)-1,2-bis(4-chlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 10 (30) N-(piperidin-1-yl)-1,2-bis(4-chlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (31) N-(cyclohexyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
- 15 (32) N-(piperidin-1-yl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
- (33) N-(cyclohexyl)-1-(4-bromophenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
- (34) N-(piperidin-1-yl)-1-(4-bromophenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
- 20 (35) N-(cyclohexyl)-1-(4-isopropylphenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
- (36) N-(piperidin-1-yl)-1-(4-isopropylphenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
- 25 (37) N-(cyclohexyl)-1-(3-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (38) N-(cyclohexyl)-1-(4-chlorophenyl)-2-(2-chloro-4-fluorophenyl)-5-methyl-imidazole-4-carboxamide;
- (39) N-(piperidin-1-yl)-1-(4-chlorophenyl)-2-(2-chloro-4-fluorophenyl)-5-methyl-imidazole-4-carboxamide;
- 30 (40) N-(cyclohexyl)-1-(2-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide; and
- (41) N-(cyclohexyl)-1-(4-chlorophenyl)-2-(3-chlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 35 or a pharmaceutically acceptable salt thereof.

11. The method according to Claim 10, wherein the compound of structural formula I is selected from:

- 5 (1) N-(cyclohexyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
 - (2) N-(piperidin-1-yl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
 - (3) N-(cyclohexyl)-1-(4-bromophenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
 - 10 (4) N-(cyclohexyl)-1-(4-isopropylphenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
 - (5) N-(cyclohexyl)-1-(4-bromophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide; and
 - 15 (6) N-(cycloheptyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- or a pharmaceutically acceptable salt thereof.

12. A method of preventing obesity in a person at risk for obesity comprising administration to said person of about 0.001 mg to about 100 mg per kg of
20 a compound of structural formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

R¹ is selected from:

- 25 (1) hydrogen,
- (2) C₁₋₄alkyl,
- (3) C₂₋₄alkenyl,
- (4) C₂₋₄alkynyl,
- (5) C₃₋₇cycloalkyl,

- (6) C₃₋₇cycloalkyl-C₁₋₄alkyl,
- (7) cycloheteroalkyl,
- (8) cycloheteroalkyl-C₁₋₄alkyl,
- (9) aryl, and
- 5 (10) heteroaryl;

wherein alkyl, alkenyl, alkynyl, cycloalkyl, and cycloheteroalkyl are optionally substituted with one to four substituents independently selected from R^a, and aryl and heteroaryl are optionally substituted with one to four substituents independently selected from R^b;

10 R² is selected from:

- (1) -OR^c,
- (2) -OC(O)R^c,
- (3) -OC(O)NR^cR^d,
- (4) -SR^c,
- 15 (5) -S(O)_mR^c,
- (6) -SO₂NR^cR^d,
- (7) -NR^cR^d,
- (8) -NR^cC(O)R^d,
- (9) -NR^cSO₂R^d,
- 20 (10) -NR^cC(O)NR^cR^d,
- (11) -NR^cC(O)OR^d,
- (12) -C(O)OR^c, and
- (13) -C(O)NR^cR^d;

R³ is selected from:

- 25 (1) -C₁₋₁₀alkyl, and
- (2) -Ar²;

Ar¹ and Ar² are independently selected from phenyl, naphthyl, thienyl, furanyl, pyrrolyl, benzothienyl, benzofuranyl, indanyl, indenyl, indolyl, tetrahydronaphthyl, 2,3-dihydrobenzofuranyl, dihydrobenzopyranyl, and 1,4-benzodioxanyl, each

30 optionally substituted with one, two, or three groups independently selected from R^b; each R^a is independently selected from:

- (1) -OR^c,
- (2) -NR^cS(O)_mR^d,
- (3) halogen,

- (4) $-S(O)_mR^c$,
 (5) $-SR^c$,
 (6) $-S(O)_2OR^c$,
 (7) $-S(O)_mNR^cR^d$,
 5 (8) $-NR^cR^d$,
 (9) $-O(CR^eR^f)_nNR^cR^d$,
 (10) $-C(O)R^c$,
 (11) $-CO_2R^c$,
 (12) $-CO_2(CR^eR^f)_nCONR^cR^d$,
 10 (13) $-OC(O)R^c$,
 (14) $-CN$,
 (15) $-C(O)NR^cR^d$,
 (16) $-NR^cC(O)R^d$,
 (17) $-OC(O)NR^cR^d$,
 15 (18) $-NR^cC(O)OR^d$,
 (19) $-NR^cC(O)NR^cR^d$,
 (20) $-CR^c(N-OR^d)$,
 (21) $-CF_3$,
 (22) $-OCF_3$,
 20 (23) C₃₋₈cycloalkyl, and
 (24) cycloheteroalkyl;

each R^b is independently selected from:

- (1) C₁₋₆alkyl,
 (2) C₂₋₆alkenyl,
 25 (3) C₂₋₆alkynyl,
 (4) $-OR^c$,
 (5) $-NR^cS(O)_mR^d$,
 (6) $-NO_2$,
 (7) halogen,
 30 (8) $-S(O)_mR^c$,
 (9) $-SR^c$,
 (10) $-S(O)_2OR^c$,
 (11) $-S(O)_mNR^cR^d$,
 (12) $-NR^cR^d$,

- (13) $-O(CR^eR^f)_nNR^cR^d$,
 (14) $-C(O)R^c$,
 (15) $-CO_2R^c$,
 (16) $-CO_2(CR^eR^f)_nCONR^cR^d$,
 5 (17) $-OC(O)R^c$,
 (18) $-CN$,
 (19) $-C(O)NR^cR^d$,
 (20) $-NR^cC(O)R^d$,
 (21) $-OC(O)NR^cR^d$,
 10 (22) $-NR^cC(O)OR^d$,
 (23) $-NR^cC(O)NR^cR^d$,
 (24) $-CR^c(N-OR^d)$,
 (25) $-CF_3$,
 (26) $-OCF_3$,
 15 (27) C_{3-8} cycloalkyl,
 (28) cycloheteroalkyl, and
 (29) phenyl;
- each R^c and R^d is independently selected from:
- (1) hydrogen,
 20 (2) C_{1-10} alkyl,
 (3) C_{2-10} alkenyl,
 (4) C_{2-10} alkynyl,
 (5) $-N(C_{1-10}alkyl)_2$,
 (6) $-NH(C_{1-10}alkyl)$,
 25 (7) cycloalkyl,
 (8) cycloalkyl- C_{1-10} alkyl;
 (9) cycloheteroalkyl,
 (10) cycloheteroalkyl- C_{1-10} alkyl;
 (11) aryl,
 30 (12) heteroaryl,
 (13) aryl- C_{1-10} alkyl, and
 (14) heteroaryl- C_{1-10} alkyl, or

R^c and R^d together with the atom to which they are attached form a heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N- R^c ,

each R^c and R^d may be unsubstituted or substituted with one to three substituents

5 selected from R^e ;

each R^e and R^f is independently selected from:

- (1) hydrogen,
- (2) C_{1-10} alkyl,
- (3) C_{2-10} alkenyl,
- 10 (4) C_{2-10} alkynyl,
- (5) cycloalkyl,
- (6) cycloalkyl- C_{1-10} alkyl,
- (7) cycloheteroalkyl,
- (8) cycloheteroalkyl- C_{1-10} alkyl,
- 15 (9) aryl,
- (10) heteroaryl,
- (11) aryl- C_{1-10} alkyl, and
- (12) heteroaryl- C_{1-10} alkyl, or

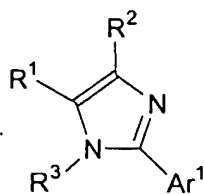
20 R^e and R^f together with the carbon to which they are attached form a ring of 5 to 7 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and nitrogen;

m is selected from 1 and 2; and

n is selected from 1, 2, and 3.

25

13. A compound of structural formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

R¹ is selected from: methyl and ethyl,
 wherein methyl and ethyl are optionally substituted with one to four substituents
 independently selected from R^a;

5 R² is selected from:

- (1) -C(O)OR^c, and
- (2) -C(O)NR^cR^d;

R³ is selected from methyl and Ar²;

Ar¹ and Ar² are phenyl, each optionally substituted with one, two, or three groups
 10 independently selected from R^b;
 each R^a is independently selected from:

- (1) -OR^c,
- (2) -NR^cS(O)_mR^d,
- (3) halogen,
- 15 (4) -S(O)_mR^c,
- (5) -SR^c,
- (6) -S(O)_mNR^cR^d,
- (7) -NR^cR^d,
- (8) -O(CR^eR^f)_nNR^cR^d,
- 20 (9) -C(O)R^c,
- (10) -CN,
- (11) -C(O)NR^cR^d,
- (12) -NR^cC(O)R^d,
- (13) -CF₃, and
- 25 (14) -OCF₃;

each R^b is independently selected from: halogen, C₁₋₃alkyl, -CN, and phenyl;

each R^c and R^d is independently selected from:

- (1) hydrogen,
- (2) C₁₋₁₀alkyl,
- 30 (3) C₂₋₁₀alkenyl,
- (4) C₂₋₁₀alkynyl,
- (5) -NH(C₁₋₁₀alkyl),
- (6) -N(C₁₋₁₀alkyl)₂,
- (7) cycloalkyl,

- 5 (8) cycloalkyl-C₁₋₁₀alkyl,
 (9) cycloheteroalkyl,
 (10) cycloheteroalkyl-C₁₋₁₀ alkyl,
 (11) aryl,
 (12) heteroaryl,
 (13) aryl-C₁₋₁₀alkyl, and
 (14) heteroaryl-C₁₋₁₀alkyl, or

R^c and R^d together with the atom to which they are attached form a heterocyclic ring
 of 4 to 7 members containing 0-2 additional heteroatoms independently selected from
 10 oxygen, sulfur and N-R^c,
 each R^c and R^d may be unsubstituted or substituted with one to three substituents
 selected from R^e;
 each R^e and R^f is independently selected from:

- 15 (1) hydrogen,
 (2) C₁₋₁₀alkyl,
 (3) C₂₋₁₀ alkenyl,
 (4) C₂₋₁₀alkynyl,
 (5) cycloalkyl,
 (6) cycloalkyl-C₁₋₁₀ alkyl,
 20 (7) cycloheteroalkyl,
 (8) cycloheteroalkyl-C₁₋₁₀ alkyl,
 (9) aryl,
 (10) heteroaryl,
 (11) aryl-C₁₋₁₀ alkyl, and
 25 (12) heteroaryl-C₁₋₁₀ alkyl, or

R^e and R^f together with the carbon to which they are attached form a ring of 5 to 7
 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and
 nitrogen;
 m is selected from 1 and 2; and
 30 n is selected from 1, 2, and 3.

14. The compound of claim 13 wherein:

R¹ is methyl;
 R² is -C(O)NR^cR^d;

R³ is selected from methyl and Ar²;

Ar¹ is phenyl substituted at the 2 and 4 positions with a substituent independently selected from R^b;

Ar² is independently selected from:

- 5 (1) phenyl,
- (2) 4-fluorophenyl,
- (3) 2-chlorophenyl,
- (4) 3-chlorophenyl,
- (5) 4-chlorophenyl,
- 10 (6) 4-cyanophenyl,
- (7) 4-methylphenyl,
- (8) 4-isopropylphenyl,
- (9) 4-biphenyl,
- (10) 4-bromophenyl,
- 15 (11) 4-iodophenyl,
- (12) 2,4-dichlorophenyl, and
- (13) 2-chloro-4-fluorophenyl;

each R^c and R^d is independently selected from:

- (1) hydrogen,
- 20 (2) methyl,
- (3) ethyl,
- (4) -N(CH₃)₂,
- (5) -NH(CH₃),
- (6) cyclopentane,
- 25 (7) cyclohexane,
- (8) cycloheptane,
- (9) piperidine
- (10) morpholine,
- (11) pyrrolidine,
- 30 (12) azepine, and
- (13) 4-methylpiperazine,

each R^c and R^d may be unsubstituted or substituted with one to three substituents selected from R^e;

or a pharmaceutically acceptable salt thereof.

15. A compound selected from:

- (1) ethyl 1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxylate;
- 5 (2) ethyl 2-(2,4-dichlorophenyl)-1,5-dimethyl-imidazole-4-carboxylate;
- (3) N-(cyclohexyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (4) N-(piperidin-1-yl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 10 (5) N-(piperidin-1-yl)-2-(2,4-dichlorophenyl)-1,5-dimethyl-imidazole-4-carboxamide;
- (6) N-(cyclopentyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (7) N-(cycloheptyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 15 (8) N-(morpholin-4-yl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (9) N-(pyrrolidin-1-yl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 20 (10) N-(azepin-1-yl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (11) N-(4-methylpiperazin-1-yl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (12) N',N'-dimethyl-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxhydrazide;
- 25 (13) N-(cyclohexyl)-1-(phenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (14) N-(piperidin-1-yl)-1-(phenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 30 (15) N-(cyclohexyl)-1-(4-fluorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (16) N-(piperidin-1-yl)-1-(4-fluorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (17) N-(4-methyl-cyclohexyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide (Isomer A);
- 35

- (18) N-(2-(pyrrolidin-1-yl)ethyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (19) N-(cyclohexyl)-1-(4-chlorophenyl)-2-(2-chlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 5 (20) N-(piperidin-1-yl)-1-(4-chlorophenyl)-2-(2-chlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (21) N-(cyclohexyl)-1-(4-bromophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (22) N-(piperidin-1-yl)-1-(4-bromophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 10 (23) N-(cyclohexyl)-1-(4-isopropylphenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (24) N-(piperidin-1-yl)-1-(4-isopropylphenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 15 (25) N-(cyclohexyl)-1-(4-cyanophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (26) N-(piperidin-1-yl)-1-(4-cyanophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (27) N-(cyclohexyl)-1-(4-biphenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 20 (28) N-(piperidin-1-yl)-1-(4-biphenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (29) N-(cyclohexyl)-1,2-bis(4-chlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 25 (30) N-(piperidin-1-yl)-1,2-bis(4-chlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (31) N-(cyclohexyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
- (32) N-(piperidin-1-yl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
- 30 (33) N-(cyclohexyl)-1-(4-bromophenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
- (34) N-(piperidin-1-yl)-1-(4-bromophenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;

- (35) N-(cyclohexyl)-1-(4-isopropylphenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
- (36) N-(piperidin-1-yl)-1-(4-isopropylphenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
- 5 (37) N-(cyclohexyl)-1-(3-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (38) N-(cyclohexyl)-1-(4-chlorophenyl)-2-(2-chloro-4-fluorophenyl)-5-methyl-imidazole-4-carboxamide;
- (39) N-(piperidin-1-yl)-1-(4-chlorophenyl)-2-(2-chloro-4-fluorophenyl)-5-methyl-imidazole-4-carboxamide;
- 10 (40) N-(cyclohexyl)-1-(2-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide; and
- (41) N-(cyclohexyl)-1-(4-chlorophenyl)-2-(3-chlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 15 or a pharmaceutically acceptable salt thereof.

16. The compound according to Claim 15 selected from:

- (1) N-(cyclohexyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 20 (2) N-(piperidin-1-yl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- (3) N-(cyclohexyl)-1-(4-bromophenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
- (4) N-(cyclohexyl)-1-(4-isopropylphenyl)-2-(2,4-dichlorophenyl)-5-ethyl-imidazole-4-carboxamide;
- 25 (5) N-(cyclohexyl)-1-(4-bromophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide; and
- (6) N-(cycloheptyl)-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-5-methyl-imidazole-4-carboxamide;
- 30 or a pharmaceutically acceptable salt thereof.

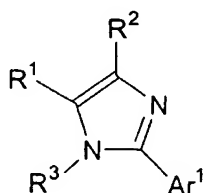
17. A composition comprising a compound according to Claim 13 and a pharmaceutically acceptable carrier.

18. A composition comprising a compound according to Claim 15 and a pharmaceutically acceptable carrier.

19. A method of preventing obesity in a person at risk for obesity comprising administration to said person of about 0.001 to about 100 mg/kg of a compound according to Claim 13.

20. A method of preventing obesity in a person at risk for obesity comprising administration to said person of about 0.001 to about 100 mg/kg of a compound according to Claim 15.

21. A composition comprising a pharmaceutically effective amount of a compound of structural formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

R¹ is selected from:

- (1) hydrogen,
- (2) C₁₋₄alkyl,
- (3) C₂₋₄alkenyl,
- (4) C₂₋₄alkynyl,
- (5) C₃₋₇cycloalkyl,
- (6) C₃₋₇cycloalkyl-C₁₋₄alkyl,
- (7) cycloheteroalkyl,
- (8) cycloheteroalkyl-C₁₋₄alkyl,
- (9) aryl, and
- (10) heteroaryl;

wherein alkyl, alkenyl, alkynyl, cycloalkyl, and cycloheteroalkyl are optionally substituted with one to four substituents independently selected from R^a , and aryl and heteroaryl are optionally substituted with one to four substituents independently selected from R^b ;

5 R^2 is selected from:

- (1) $-OR^c$,
- (2) $-OC(O)R^c$,
- (3) $-OC(O)NR^cR^d$,
- (4) $-SR^c$,
- 10 (5) $-S(O)_mR^c$,
- (6) $-SO_2NR^cR^d$,
- (7) $-NR^cR^d$,
- (8) $-NR^cC(O)R^d$,
- (9) $-NR^cSO_2R^d$,
- 15 (10) $-NR^cC(O)NR^cR^d$,
- (11) $-NR^cC(O)OR^d$,
- (12) $-C(O)OR^c$, and
- (13) $-C(O)NR^cR^d$;

R^3 is selected from:

- 20 (1) $-C_{1-10}alkyl$, and
- (2) $-Ar^2$;

Ar^1 and Ar^2 are independently selected from phenyl, naphthyl, thienyl, furanyl, pyrrolyl, benzothienyl, benzofuranyl, indanyl, indenyl, indolyl, tetrahydronaphthyl, 2,3-dihydrobenzofuranyl, dihydrobenzopyranyl, and 1,4-benzodioxanyl, each

25 optionally substituted with one, two, or three groups independently selected from R^b ; each R^a is independently selected from:

- (1) $-OR^c$,
- (2) $-NR^cS(O)_mR^d$,
- (3) halogen,
- 30 (4) $-S(O)_mR^c$,
- (5) $-SR^c$,
- (6) $-S(O)_2OR^c$,
- (7) $-S(O)_mNR^cR^d$,
- (8) $-NR^cR^d$,

- 5
- (9) $-\text{O}(\text{CR}^{\text{e}}\text{R}^{\text{f}})_n\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
 - (10) $-\text{C}(\text{O})\text{R}^{\text{c}}$,
 - (11) $-\text{CO}_2\text{R}^{\text{c}}$,
 - (12) $-\text{CO}_2(\text{CR}^{\text{e}}\text{R}^{\text{f}})_n\text{CONR}^{\text{c}}\text{R}^{\text{d}}$,
 - (13) $-\text{OC}(\text{O})\text{R}^{\text{c}}$,
 - (14) $-\text{CN}$,
 - (15) $-\text{C}(\text{O})\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
 - (16) $-\text{NR}^{\text{c}}\text{C}(\text{O})\text{R}^{\text{d}}$,
 - (17) $-\text{OC}(\text{O})\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
 - 10 (18) $-\text{NR}^{\text{c}}\text{C}(\text{O})\text{OR}^{\text{d}}$,
 - (19) $-\text{NR}^{\text{c}}\text{C}(\text{O})\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
 - (20) $-\text{CR}^{\text{c}}(\text{N}-\text{OR}^{\text{d}})$,
 - (21) $-\text{CF}_3$,
 - (22) $-\text{OCF}_3$,
 - 15 (23) C_3 -8cycloalkyl, and
 - (24) cycloheteroalkyl;

each R^{b} is independently selected from:

- (1) C_{1-6} alkyl,
- (2) C_{2-6} alkenyl,
- 20 (3) C_{2-6} alkynyl,
- (4) $-\text{OR}^{\text{c}}$,
- (5) $-\text{NR}^{\text{c}}\text{S}(\text{O})_m\text{R}^{\text{d}}$,
- (6) $-\text{NO}_2$,
- (7) halogen,
- 25 (8) $-\text{S}(\text{O})_m\text{R}^{\text{c}}$,
- (9) $-\text{SR}^{\text{c}}$,
- (10) $-\text{S}(\text{O})_2\text{OR}^{\text{c}}$,
- (11) $-\text{S}(\text{O})_m\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
- (12) $-\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
- 30 (13) $-\text{O}(\text{CR}^{\text{e}}\text{R}^{\text{f}})_n\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
- (14) $-\text{C}(\text{O})\text{R}^{\text{c}}$,
- (15) $-\text{CO}_2\text{R}^{\text{c}}$,
- (16) $-\text{CO}_2(\text{CR}^{\text{e}}\text{R}^{\text{f}})_n\text{CONR}^{\text{c}}\text{R}^{\text{d}}$,
- (17) $-\text{OC}(\text{O})\text{R}^{\text{c}}$,

- 5
- (18) -CN,
 - (19) -C(O)NR^cR^d,
 - (20) -NR^cC(O)R^d,
 - (21) -OC(O)NR^cR^d,
 - (22) -NR^cC(O)OR^d,
 - (23) -NR^cC(O)NR^cR^d,
 - (24) -CR^c(N-OR^d),
 - (25) -CF₃,
 - (26) -OCF₃,
 - 10 (27) C₃-8cycloalkyl,
 - (28) cycloheteroalkyl, and
 - (29) phenyl;

each R^c and R^d is independently selected from:

- 15
- (1) hydrogen,
 - (2) C₁-10alkyl,
 - (3) C₂-10 alkenyl,
 - (4) C₂-10alkynyl,
 - (5) -NH(C₁-10alkyl),
 - (6) -N(C₁-10alkyl)₂,
 - 20 (7) cycloalkyl,
 - (8) cycloalkyl-C₁-10alkyl;
 - (9) cycloheteroalkyl,
 - (10) cycloheteroalkyl-C₁-10 alkyl;
 - (11) aryl,
 - 25 (12) heteroaryl,
 - (13) aryl-C₁-10alkyl, and
 - (14) heteroaryl-C₁-10alkyl, or

R^c and R^d together with the atom to which they are attached form a heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from

30 oxygen, sulfur and N-R^c,

each R^c and R^d may be unsubstituted or substituted with one to three substituents selected from R^e;

each R^e and R^f is independently selected from:

- (1) hydrogen,

- (2) C₁₋₁₀alkyl,
 (3) C₂₋₁₀alkenyl,
 (4) C₂₋₁₀alkynyl,
 (5) cycloalkyl,
 5 (6) cycloalkyl-C₁₋₁₀ alkyl,
 (7) cycloheteroalkyl,
 (8) cycloheteroalkyl-C₁₋₁₀ alkyl,
 (9) aryl,
 (10) heteroaryl,
 10 (11) aryl-C₁₋₁₀ alkyl, and
 (12) heteroaryl-C₁₋₁₀ alkyl, or

R^e and R^f together with the carbon to which they are attached form a ring of 5 to 7 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and nitrogen;

- 15 m is selected from 1 and 2; and
 n is selected from 1, 2, and 3;

and an anorectic agent selected from: aminorex, amphechloral, amphetamine, benzphetamine, chlorphentermine, clobenzorex, cloforex, clominorex, clortermine, cyclixedrine, dexfenfluramine, dextroamphetamine, diethylpropion,

- 20 diphenmethoxidine, *N*-ethylamphetamine, fenbutrazate, fenfluramine, fenisorex, fenproporex, fludorex, fluminorex, furfurylmethylamphetamine, levamfetamine, levophacetoperane, mazindol, mefenorex, metamfepramone, methamphetamine, norpseudoephedrine, pentorex, phendimetrazine, phenmetrazine, phentermine, phenylpropanolamine, picilorex and sibutramine; or

- 25 a selective serotonin reuptake inhibitor selected from: fluoxetine, fluvoxamine, paroxetine and sertraline;
 and a pharmaceutically acceptable carrier.

- 30 22. A composition comprising a pharmaceutically effective amount of
 a compound of structural formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

R¹ is selected from:

- 5 (1) hydrogen,
- (2) C₁₋₄alkyl,
- (3) C₂₋₄alkenyl,
- (4) C₂₋₄alkynyl,
- (5) C₃₋₇cycloalkyl,
- 10 (6) C₃₋₇cycloalkyl-C₁₋₄alkyl,
- (7) cycloheteroalkyl,
- (8) cycloheteroalkyl-C₁₋₄alkyl,
- (9) aryl, and
- (10) heteroaryl;

- 15 wherein alkyl, alkenyl, alkynyl, cycloalkyl, and cycloheteroalkyl are optionally substituted with one to four substituents independently selected from R^a, and aryl and heteroaryl are optionally substituted with one to four substituents independently selected from R^b;

R² is selected from:

- 20 (1) -OR^c,
- (2) -OC(O)R^c,
- (3) -OC(O)NR^cR^d,
- (4) -SR^c,
- (5) -S(O)_mR^c,
- 25 (6) -SO₂NR^cR^d,
- (7) -NR^cR^d,
- (8) -NR^cC(O)R^d,
- (9) -NR^cSO₂R^d,
- (10) -NR^cC(O)NR^cR^d,
- 30 (11) -NR^cC(O)OR^d,

(12) $-\text{C}(\text{O})\text{OR}^c$, and

(13) $-\text{C}(\text{O})\text{NR}^c\text{R}^d$;

R^3 is selected from:

(1) $-\text{C}_{1-10}\text{alkyl}$, and

5 (2) $-\text{Ar}^2$;

Ar^1 and Ar^2 are independently selected from phenyl, naphthyl, thienyl, furanyl, pyrrolyl, benzothienyl, benzofuranyl, indanyl, indenyl, indolyl, tetrahydronaphthyl, 2,3-dihydrobenzofuranyl, dihydrobenzopyranyl, and 1,4-benzodioxanyl, each optionally substituted with one, two, or three groups independently selected from R^b ;

10 each R^a is independently selected from:

(1) $-\text{OR}^c$,

(2) $-\text{NR}^c\text{S}(\text{O})_m\text{R}^d$,

(3) halogen,

(4) $-\text{S}(\text{O})_m\text{R}^c$,

15 (5) $-\text{SR}^c$,

(6) $-\text{S}(\text{O})_2\text{OR}^c$,

(7) $-\text{S}(\text{O})_m\text{NR}^c\text{R}^d$,

(8) $-\text{NR}^c\text{R}^d$,

(9) $-\text{O}(\text{CR}^e\text{R}^f)_n\text{NR}^c\text{R}^d$,

20 (10) $-\text{C}(\text{O})\text{R}^c$,

(11) $-\text{CO}_2\text{R}^c$,

(12) $-\text{CO}_2(\text{CR}^e\text{R}^f)_n\text{CONR}^c\text{R}^d$,

(13) $-\text{OC}(\text{O})\text{R}^c$,

(14) $-\text{CN}$,

25 (15) $-\text{C}(\text{O})\text{NR}^c\text{R}^d$,

(16) $-\text{NR}^c\text{C}(\text{O})\text{R}^d$,

(17) $-\text{OC}(\text{O})\text{NR}^c\text{R}^d$,

(18) $-\text{NR}^c\text{C}(\text{O})\text{OR}^d$,

(19) $-\text{NR}^c\text{C}(\text{O})\text{NR}^c\text{R}^d$,

30 (20) $-\text{CR}^c(\text{N}-\text{OR}^d)$,

(21) $-\text{CF}_3$,

(22) $-\text{OCF}_3$,

(23) $\text{C}_{3-8}\text{cycloalkyl}$, and

(24) cycloheteroalkyl;

each R^b is independently selected from:

- (1) C_{1-6} alkyl,
- (2) C_{2-6} alkenyl,
- (3) C_{2-6} alkynyl,
- 5 (4) $-OR^c$,
- (5) $-NR^cS(O)_mR^d$,
- (6) $-NO_2$,
- (7) halogen,
- (8) $-S(O)_mR^c$,
- 10 (9) $-SR^c$,
- (10) $-S(O)_2OR^c$,
- (11) $-S(O)_mNR^cR^d$,
- (12) $-NR^cR^d$,
- (13) $-O(CR^eR^f)_nNR^cR^d$,
- 15 (14) $-C(O)R^c$,
- (15) $-CO_2R^c$,
- (16) $-CO_2(CR^eR^f)_nCONR^cR^d$,
- (17) $-OC(O)R^c$,
- (18) $-CN$,
- 20 (19) $-C(O)NR^cR^d$,
- (20) $-NR^cC(O)R^d$,
- (21) $-OC(O)NR^cR^d$,
- (22) $-NR^cC(O)OR^d$,
- (23) $-NR^cC(O)NR^cR^d$,
- 25 (24) $-CR^c(N-OR^d)$,
- (25) $-CF_3$,
- (26) $-OCF_3$,
- (27) C_{3-8} cycloalkyl, and
- (28) cycloheteroalkyl,
- 30 (29) phenyl;

each R^c and R^d is independently selected from:

- (1) hydrogen,
- (2) C_{1-10} alkyl,
- (3) C_{2-10} alkenyl,

- (4) C₂₋₁₀alkynyl,
- (5) -NH(C₁₋₁₀alkyl),
- (6) -N(C₁₋₁₀alkyl)₂,
- (7) cycloalkyl,
- 5 (8) cycloalkyl-C₁₋₁₀alkyl;
- (9) cycloheteroalkyl,
- (10) cycloheteroalkyl-C₁₋₁₀alkyl;
- (11) aryl,
- (12) heteroaryl,
- 10 (13) aryl-C₁₋₁₀alkyl, and
- (14) heteroaryl-C₁₋₁₀alkyl, or

R^c and R^d together with the atom to which they are attached form a heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-R^c,

- 15 each R^c and R^d may be unsubstituted or substituted with one to three substituents selected from R^e;

each R^e and R^f is independently selected from:

- (1) hydrogen,
- (2) C₁₋₁₀alkyl,
- 20 (3) C₂₋₁₀alkenyl,
- (4) C₂₋₁₀alkynyl,
- (5) cycloalkyl,
- (6) cycloalkyl-C₁₋₁₀alkyl,
- (7) cycloheteroalkyl,
- 25 (8) cycloheteroalkyl-C₁₋₁₀alkyl,
- (9) aryl,
- (10) heteroaryl,
- (11) aryl-C₁₋₁₀alkyl, and
- (12) heteroaryl-C₁₋₁₀alkyl, or

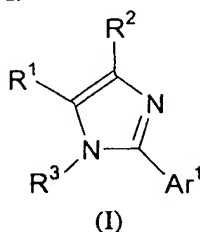
- 30 R^e and R^f together with the carbon to which they are attached form a ring of 5 to 7 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and nitrogen;

m is selected from 1 and 2; and

n is selected from 1, 2, and 3;

- and an antidepressant agent selected from: norepinephrine reuptake inhibitors, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, reversible inhibitors of monoamine oxidase, serotonin and noradrenaline reuptake inhibitors, corticotropin releasing factor antagonists, α -adrenoreceptor antagonists and atypical anti-depressants;
- 5 and a pharmaceutically acceptable carrier.

23. A composition comprising a pharmaceutically effective amount of a compound of structural formula I:



or a pharmaceutically acceptable salt thereof, wherein:

R¹ is selected from:

- (1) hydrogen,
- (2) C₁₋₄alkyl,
- (3) C₂₋₄alkenyl,
- (4) C₂₋₄alkynyl,
- (5) C₃₋₇cycloalkyl,
- (6) C₃₋₇cycloalkyl-C₁₋₄alkyl,
- (7) cycloheteroalkyl,
- (8) cycloheteroalkyl-C₁₋₄alkyl,
- (9) aryl, and
- (10) heteroaryl;

wherein alkyl, alkenyl, alkynyl, cycloalkyl, and cycloheteroalkyl are optionally substituted with one to four substituents independently selected from R^a, and aryl and heteroaryl are optionally substituted with one to four substituents independently selected from R^b;

R² is selected from:

- (1) -OR^c,
- (2) -OC(O)R^c,
- (3) -OC(O)NR^cR^d,

- (4) $-SR^c$,
 (5) $-S(O)_mR^c$,
 (6) $-SO_2NR^cR^d$,
 (7) $-NR^cR^d$,
 5 (8) $-NR^cC(O)R^d$,
 (9) $-NR^cSO_2R^d$,
 (10) $-NR^cC(O)NR^cR^d$,
 (11) $-NR^cC(O)OR^d$,
 (12) $-C(O)OR^c$, and
 10 (13) $-C(O)NR^cR^d$;

R^3 is selected from:

- (1) $-C_{1-10}alkyl$, and
 (2) $-Ar^2$;

Ar^1 and Ar^2 are independently selected from phenyl, naphthyl, thienyl, furanyl,
 15 pyrrolyl, benzothieryl, benzofuranyl, indanyl, indenyl, indolyl, tetrahydronaphthyl,
 2,3-dihydrobenzofuranyl, dihydrobenzopyranyl, and 1,4-benzodioxanyl, each
 optionally substituted with one, two, or three groups independently selected from R^b ;
 each R^a is independently selected from:

- (1) $-OR^c$,
 20 (2) $-NR^cS(O)_mR^d$,
 (3) halogen,
 (4) $-S(O)_mR^c$,
 (5) $-SR^c$,
 (6) $-S(O)_2OR^c$,
 25 (7) $-S(O)_mNR^cR^d$,
 (8) $-NR^cR^d$,
 (9) $-O(CR^eR^f)_nNR^cR^d$,
 (10) $-C(O)R^c$,
 (11) $-CO_2R^c$,
 30 (12) $-CO_2(CR^eR^f)_nCONR^cR^d$,
 (13) $-OC(O)R^c$,
 (14) $-CN$,
 (15) $-C(O)NR^cR^d$,
 (16) $-NR^cC(O)R^d$,

- (17) $-\text{OC}(\text{O})\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
 (18) $-\text{NR}^{\text{c}}\text{C}(\text{O})\text{OR}^{\text{d}}$,
 (19) $-\text{NR}^{\text{c}}\text{C}(\text{O})\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
 (20) $-\text{CR}^{\text{c}}(\text{N}-\text{OR}^{\text{d}})$,
 5 (21) $-\text{CF}_3$,
 (22) $-\text{OCF}_3$,
 (23) C_3 -8cycloalkyl, and
 (24) cycloheteroalkyl;
 each R^{b} is independently selected from:
- 10 (1) C_{1-6} alkyl,
 (2) C_{2-6} alkenyl,
 (3) C_{2-6} alkynyl,
 (4) $-\text{OR}^{\text{c}}$,
 (5) $-\text{NR}^{\text{c}}\text{S}(\text{O})_{\text{m}}\text{R}^{\text{d}}$,
 15 (6) $-\text{NO}_2$,
 (7) halogen,
 (8) $-\text{S}(\text{O})_{\text{m}}\text{R}^{\text{c}}$,
 (9) $-\text{SR}^{\text{c}}$,
 (10) $-\text{S}(\text{O})_2\text{OR}^{\text{c}}$,
 20 (11) $-\text{S}(\text{O})_{\text{m}}\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
 (12) $-\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
 (13) $-\text{O}(\text{CR}^{\text{e}}\text{R}^{\text{f}})_n\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
 (14) $-\text{C}(\text{O})\text{R}^{\text{c}}$,
 (15) $-\text{CO}_2\text{R}^{\text{c}}$,
 25 (16) $-\text{CO}_2(\text{CR}^{\text{e}}\text{R}^{\text{f}})_n\text{CONR}^{\text{c}}\text{R}^{\text{d}}$,
 (17) $-\text{OC}(\text{O})\text{R}^{\text{c}}$,
 (18) $-\text{CN}$,
 (19) $-\text{C}(\text{O})\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
 (20) $-\text{NR}^{\text{c}}\text{C}(\text{O})\text{R}^{\text{d}}$,
 30 (21) $-\text{OC}(\text{O})\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
 (22) $-\text{NR}^{\text{c}}\text{C}(\text{O})\text{OR}^{\text{d}}$,
 (23) $-\text{NR}^{\text{c}}\text{C}(\text{O})\text{NR}^{\text{c}}\text{R}^{\text{d}}$,
 (24) $-\text{CR}^{\text{c}}(\text{N}-\text{OR}^{\text{d}})$,
 (25) $-\text{CF}_3$,

- (26) -OCF₃,
 - (27) C₃₋₈cycloalkyl,
 - (28) cycloheteroalkyl, and
 - (29) phenyl;
- 5 each R^c and R^d is independently selected from:
- (1) hydrogen,
 - (2) C₁₋₁₀alkyl,
 - (3) C₂₋₁₀alkenyl,
 - (4) C₂₋₁₀alkynyl,
 - 10 (5) -NH(C₁₋₁₀alkyl),
 - (6) -N(C₁₋₁₀alkyl)₂,
 - (7) cycloalkyl,
 - (8) cycloalkyl-C₁₋₁₀alkyl;
 - (9) cycloheteroalkyl,
 - 15 (10) cycloheteroalkyl-C₁₋₁₀alkyl;
 - (11) aryl,
 - (12) heteroaryl,
 - (13) aryl-C₁₋₁₀alkyl, and
 - (14) heteroaryl-C₁₋₁₀alkyl, or
- 20 R^c and R^d together with the atom to which they are attached form a heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-R^c,
- each R^c and R^d may be unsubstituted or substituted with one to three substituents selected from R^e;
- 25 each R^e and R^f is independently selected from:
- (1) hydrogen,
 - (2) C₁₋₁₀alkyl,
 - (3) C₂₋₁₀alkenyl,
 - (4) C₂₋₁₀alkynyl,
 - 30 (5) cycloalkyl,
 - (6) cycloalkyl-C₁₋₁₀alkyl,
 - (7) cycloheteroalkyl,
 - (8) cycloheteroalkyl-C₁₋₁₀alkyl,
 - (9) aryl,

- (10) heteroaryl,
- (11) aryl-C₁₋₁₀ alkyl, and
- (12) heteroaryl-C₁₋₁₀ alkyl, or

5 R^e and R^f together with the carbon to which they are attached form a ring of 5 to 7 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and nitrogen;
 m is selected from 1 and 2; and
 n is selected from 1, 2, and 3;
 and the VLA-4 antagonist natalizumab; or a steroid or corticosteroid selected from:
 10 beclomethasone, methylprednisolone, betamethasone, prednisone, dexamethasone, and hydrocortisone; or an antihistamine selected from: bromopheniramine, chlorpheniramine, dexchlorpheniramine, triprolidine, clemastine, diphenhydramine, diphenylpyraline, tripeleminamine, hydroxyzine, methdilazine, promethazine, trimeprazine, azatadine, cyproheptadine, antazoline, pheniramine pyrilamine,
 15 astemizole, terfenadine, loratadine, desloratadine, cetirizine, fexofenadine, and descarboethoxyloratadine; or a non-steroidal anti-asthmatics selected from: theophylline, cromolyn sodium, atropine, and ipratropium bromide; or a β 2-agonist selected from: terbutaline, metaproterenol, fenoterol, isoetharine, albuterol, bitolterol, salmeterol, epinephrine, and pirbuterol; or a leukotriene antagonist selected from:
 20 zafirlukast, montelukast, pranlukast, iralukast, pobilukast, and SKB-106,203; or a leukotriene biosynthesis inhibitors selected from: zileuton, and BAY-1005; or an anti-cholinergic agent selected from ipratropium bromide and atropine; or an antagonist of the CCR-3 chemokine receptors;
 and a pharmaceutically acceptable carrier.

25

24. A composition comprising a pharmaceutically effective amount of a compound of structural formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

R¹ is selected from:

- (1) hydrogen,
- 5 (2) C₁₋₄alkyl,
- (3) C₂₋₄alkenyl,
- (4) C₂₋₄alkynyl,
- (5) C₃₋₇cycloalkyl,
- (6) C₃₋₇cycloalkyl-C₁₋₄alkyl,
- 10 (7) cycloheteroalkyl,
- (8) cycloheteroalkyl-C₁₋₄alkyl,
- (9) aryl, and
- (10) heteroaryl;

wherein alkyl, alkenyl, alkynyl, cycloalkyl, and cycloheteroalkyl are optionally
 15 substituted with one to four substituents independently selected from R^a, and aryl and
 heteroaryl are optionally substituted with one to four substituents independently
 selected from R^b;

R² is selected from:

- (1) -OR^c,
- 20 (2) -OC(O)R^c,
- (3) -OC(O)NR^cR^d,
- (4) -SR^c,
- (5) -S(O)_mR^c,
- (6) -SO₂NR^cR^d,
- 25 (7) -NR^cR^d,
- (8) -NR^cC(O)R^d,
- (9) -NR^cSO₂R^d,
- (10) -NR^cC(O)NR^cR^d,
- (11) -NR^cC(O)OR^d,
- 30 (12) -C(O)OR^c, and
- (13) -C(O)NR^cR^d;

R³ is selected from:

- (1) -C₁₋₁₀alkyl, and
- (2) -Ar²;

Ar¹ and Ar² are independently selected from phenyl, naphthyl, thienyl, furanyl, pyrrolyl, benzothienyl, benzofuranyl, indanyl, indenyl, indolyl, tetrahydronaphthyl, 2,3-dihydrobenzofuranyl, dihydrobenzopyranyl, and 1,4-benzodioxanyl, each optionally substituted with one, two, or three groups independently selected from R^b;

5 each R^a is independently selected from:

- (1) -OR^c,
- (2) -NR^cS(O)_mR^d,
- (3) halogen,
- (4) -S(O)_mR^c,
- 10 (5) -SR^c,
- (6) -S(O)₂OR^c,
- (7) -S(O)_mNR^cR^d,
- (8) -NR^cR^d,
- (9) -O(CR^eR^f)_nNR^cR^d,
- 15 (10) -C(O)R^c,
- (11) -CO₂R^c,
- (12) -CO₂(CR^eR^f)_nCONR^cR^d,
- (13) -OC(O)R^c,
- (14) -CN,
- 20 (15) -C(O)NR^cR^d,
- (16) -NR^cC(O)R^d,
- (17) -OC(O)NR^cR^d,
- (18) -NR^cC(O)OR^d,
- (19) -NR^cC(O)NR^cR^d,
- 25 (20) -CR^c(N-OR^d),
- (21) -CF₃,
- (22) -OCF₃,
- (23) C₃₋₈cycloalkyl, and
- (24) cycloheteroalkyl;

30 each R^b is independently selected from:

- (1) C₁₋₆alkyl,
- (2) C₂₋₆alkenyl,
- (3) C₂₋₆alkynyl,
- (4) -OR^c,

- (5) $-NR^cS(O)_mR^d$,
 (6) $-NO_2$,
 (7) halogen,
 (8) $-S(O)_mR^c$,
 5 (9) $-SR^c$,
 (10) $-S(O)_2OR^c$,
 (11) $-S(O)_mNR^cR^d$,
 (12) $-NR^cR^d$,
 (13) $-O(CR^eR^f)_nNR^cR^d$,
 10 (14) $-C(O)R^c$,
 (15) $-CO_2R^c$,
 (16) $-CO_2(CR^eR^f)_nCONR^cR^d$,
 (17) $-OC(O)R^c$,
 (18) $-CN$,
 15 (19) $-C(O)NR^cR^d$,
 (20) $-NR^cC(O)R^d$,
 (21) $-OC(O)NR^cR^d$,
 (22) $-NR^cC(O)OR^d$,
 (23) $-NR^cC(O)NR^cR^d$,
 20 (24) $-CR^c(N-OR^d)$,
 (25) $-CF_3$,
 (26) $-OCF_3$,
 (27) C_3 -8cycloalkyl,
 (28) cycloheteroalkyl, and
 25 (29) phenyl;
 each R^c and R^d is independently selected from:
 (1) hydrogen,
 (2) C_1 -10alkyl,
 (3) C_2 -10 alkenyl,
 30 (4) C_2 -10alkynyl,
 (5) $-NH(C_1$ -10alkyl),
 (6) $-N(C_1$ -10alkyl)₂,
 (7) cycloalkyl,
 (8) cycloalkyl- C_1 -10alkyl;

- (9) cycloheteroalkyl,
- (10) cycloheteroalkyl-C₁₋₁₀ alkyl,
- (11) aryl,
- (12) heteroaryl,
- 5 (13) aryl-C₁₋₁₀alkyl, and
- (14) heteroaryl-C₁₋₁₀alkyl, or

R^c and R^d together with the atom to which they are attached form a heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-R^c,

- 10 each R^c and R^d may be unsubstituted or substituted with one to three substituents selected from R^e;

each R^e and R^f is independently selected from:

- (1) hydrogen,
- (2) C₁₋₁₀alkyl,
- 15 (3) C₂₋₁₀ alkenyl,
- (4) C₂₋₁₀alkynyl,
- (5) cycloalkyl,
- (6) cycloalkyl-C₁₋₁₀ alkyl,
- (7) cycloheteroalkyl,
- 20 (8) cycloheteroalkyl-C₁₋₁₀ alkyl,
- (9) aryl,
- (10) heteroaryl,
- (11) aryl-C₁₋₁₀ alkyl, and
- (12) heteroaryl-C₁₋₁₀ alkyl, or

- 25 R^e and R^f together with the carbon to which they are attached form a ring of 5 to 7 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and nitrogen;

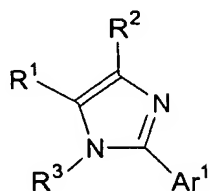
m is selected from 1 and 2; and

n is selected from 1, 2, and 3;

- 30 and an osmotic agent selected from sorbitol, lactulose, polyethylene glycol, magnesium, phosphate, and sulfate; or a laxative selected from: magnesium and docusate sodium; or a bulking agent selected from: psyllium, methylcellulose, and calcium polycarbophil; or a stimulant selected from an anthroquinone, and phenolphthalein;

and a pharmaceutically acceptable carrier.

25. A composition comprising a pharmaceutically effective amount of a compound of structural formula I:



5

(I)

or a pharmaceutically acceptable salt thereof, wherein:

R¹ is selected from:

- (1) hydrogen,
- 10 (2) C₁-4alkyl,
- (3) C₂-4alkenyl,
- (4) C₂-4alkynyl,
- (5) C₃-7cycloalkyl,
- (6) C₃-7cycloalkyl-C₁-4alkyl,
- 15 (7) cycloheteroalkyl,
- (8) cycloheteroalkyl-C₁-4alkyl,
- (9) aryl, and
- (10) heteroaryl;

20 wherein alkyl, alkenyl, alkynyl, cycloalkyl, and cycloheteroalkyl are optionally substituted with one to four substituents independently selected from R^a, and aryl and heteroaryl are optionally substituted with one to four substituents independently selected from R^b;

R² is selected from:

- (1) -OR^c,
- 25 (2) -OC(O)R^c,
- (3) -OC(O)NR^cR^d,
- (4) -SR^c,
- (5) -S(O)_mR^c,
- (6) -SO₂NR^cR^d,

- (7) $-NR^cR^d$,
 (8) $-NR^cC(O)R^d$,
 (9) $-NR^cSO_2R^d$,
 (10) $-NR^cC(O)NR^cR^d$,
 5 (11) $-NR^cC(O)OR^d$,
 (12) $-C(O)OR^c$, and
 (13) $-C(O)NR^cR^d$;

R^3 is selected from:

- (1) $-C_{1-10}alkyl$, and
 10 (2) $-Ar^2$;

Ar^1 and Ar^2 are independently selected from phenyl, naphthyl, thienyl, furanyl, pyrrolyl, benzothienyl, benzofuranyl, indanyl, indenyl, indolyl, tetrahydronaphthyl, 2,3-dihydrobenzofuranyl, dihydrobenzopyranyl, and 1,4-benzodioxanyl, each optionally substituted with one, two, or three groups independently selected from R^b ;

15 each R^a is independently selected from:

- (1) $-OR^c$,
 (2) $-NR^cS(O)_mR^d$,
 (3) halogen,
 (4) $-S(O)_mR^c$,
 20 (5) $-SR^c$,
 (6) $-S(O)_2OR^c$,
 (7) $-S(O)_mNR^cR^d$,
 (8) $-NR^cR^d$,
 (9) $-O(CR^eR^f)_nNR^cR^d$,
 25 (10) $-C(O)R^c$,
 (11) $-CO_2R^c$,
 (12) $-CO_2(CR^eR^f)_nCONR^cR^d$,
 (13) $-OC(O)R^c$,
 (14) $-CN$,
 30 (15) $-C(O)NR^cR^d$,
 (16) $-NR^cC(O)R^d$,
 (17) $-OC(O)NR^cR^d$,
 (18) $-NR^cC(O)OR^d$,
 (19) $-NR^cC(O)NR^cR^d$,

- (20) $-\text{CR}^c(\text{N}-\text{OR}^d)$,
 (21) $-\text{CF}_3$,
 (22) $-\text{OCF}_3$,
 (23) C_3 -gycloalkyl, and
 5 (24) cycloheteroalkyl;
 each R^b is independently selected from:
- (1) C_1 -alkyl,
 (2) C_2 -alkenyl,
 (3) C_2 -alkynyl,
 10 (4) $-\text{OR}^c$,
 (5) $-\text{NR}^c\text{S}(\text{O})_m\text{R}^d$,
 (6) $-\text{NO}_2$,
 (7) halogen,
 (8) $-\text{S}(\text{O})_m\text{R}^c$,
 15 (9) $-\text{SR}^c$,
 (10) $-\text{S}(\text{O})_2\text{OR}^c$,
 (11) $-\text{S}(\text{O})_m\text{NR}^c\text{R}^d$,
 (12) $-\text{NR}^c\text{R}^d$,
 (13) $-\text{O}(\text{CR}^e\text{R}^f)_n\text{NR}^c\text{R}^d$,
 20 (14) $-\text{C}(\text{O})\text{R}^c$,
 (15) $-\text{CO}_2\text{R}^c$,
 (16) $-\text{CO}_2(\text{CR}^e\text{R}^f)_n\text{CONR}^c\text{R}^d$,
 (17) $-\text{OC}(\text{O})\text{R}^c$,
 (18) $-\text{CN}$,
 25 (19) $-\text{C}(\text{O})\text{NR}^c\text{R}^d$,
 (20) $-\text{NR}^c\text{C}(\text{O})\text{R}^d$,
 (21) $-\text{OC}(\text{O})\text{NR}^c\text{R}^d$,
 (22) $-\text{NR}^c\text{C}(\text{O})\text{OR}^d$,
 (23) $-\text{NR}^c\text{C}(\text{O})\text{NR}^c\text{R}^d$,
 30 (24) $-\text{CR}^c(\text{N}-\text{OR}^d)$,
 (25) $-\text{CF}_3$,
 (26) $-\text{OCF}_3$,
 (27) C_3 -gycloalkyl,
 (28) cycloheteroalkyl, and

(29) phenyl;

each R^c and R^d is independently selected from:

- (1) hydrogen,
- (2) C₁₋₁₀alkyl,
- 5 (3) C₂₋₁₀ alkenyl,
- (4) C₂₋₁₀alkynyl,
- (5) -NH(C₁₋₁₀alkyl),
- (6) -N(C₁₋₁₀alkyl)₂,
- (7) cycloalkyl,
- 10 (8) cycloalkyl-C₁₋₁₀alkyl;
- (9) cycloheteroalkyl,
- (10) cycloheteroalkyl-C₁₋₁₀alkyl;
- (11) aryl,
- (12) heteroaryl,
- 15 (13) aryl-C₁₋₁₀alkyl, and
- (14) heteroaryl-C₁₋₁₀alkyl, or

R^c and R^d together with the atom to which they are attached form a heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-R^c,

20 each R^c and R^d may be unsubstituted or substituted with one to three substituents selected from R^e;

each R^e and R^f is independently selected from:

- (1) hydrogen,
- (2) C₁₋₁₀alkyl,
- 25 (3) C₂₋₁₀ alkenyl,
- (4) C₂₋₁₀alkynyl,
- (5) cycloalkyl,
- (6) cycloalkyl-C₁₋₁₀alkyl,
- (7) cycloheteroalkyl,
- 30 (8) cycloheteroalkyl-C₁₋₁₀alkyl,
- (9) aryl,
- (10) heteroaryl,
- (11) aryl-C₁₋₁₀alkyl, and
- (12) heteroaryl-C₁₋₁₀alkyl, or

R^e and R^f together with the carbon to which they are attached form a ring of 5 to 7 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and nitrogen;

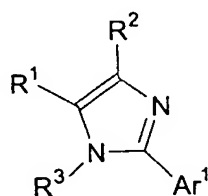
m is selected from 1 and 2; and

5 n is selected from 1, 2, and 3;

and a corticosteroid; or penicillamine; or colchicine; or an interferon- γ , 2-oxoglutarate analog; or a prostaglandin analog; or an anti-inflammatory drug selected from: azathioprine, methotrexate, leflunamide, indomethacin, and naproxen; and a pharmaceutically acceptable carrier.

10

26. The use of a compound according to of structural formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

15 R^1 is selected from:

- (1) hydrogen,
- (2) C_{1-4} alkyl,
- (3) C_{2-4} alkenyl,
- (4) C_{2-4} alkynyl,
- 20 (5) C_{3-7} cycloalkyl,
- (6) C_{3-7} cycloalkyl- C_{1-4} alkyl,
- (7) cycloheteroalkyl,
- (8) cycloheteroalkyl- C_{1-4} alkyl,
- (9) aryl, and
- 25 (10) heteroaryl;

wherein alkyl, alkenyl, alkynyl, cycloalkyl, and cycloheteroalkyl are optionally substituted with one to four substituents independently selected from R^a , and aryl and heteroaryl are optionally substituted with one to four substituents independently selected from R^b ;

R² is selected from:

- (1) -OR^c,
- (2) -OC(O)R^c,
- (3) -OC(O)NR^cR^d,
- 5 (4) -SR^c,
- (5) -S(O)_mR^c,
- (6) -SO₂NR^cR^d,
- (7) -NR^cR^d,
- (8) -NR^cC(O)R^d,
- 10 (9) -NR^cSO₂R^d,
- (10) -NR^cC(O)NR^cR^d,
- (11) -NR^cC(O)OR^d,
- (12) -C(O)OR^c, and
- (13) -C(O)NR^cR^d;

15 R³ is selected from:

- (1) -C₁₋₁₀alkyl, and
- (2) -Ar²;

Ar¹ and Ar² are independently selected from phenyl, naphthyl, thienyl, furanyl, pyrrolyl, benzothienyl, benzofuranyl, indanyl, indenyl, indolyl, tetrahydronaphthyl, 20 2,3-dihydrobenzofuranyl, dihydrobenzopyranyl, and 1,4-benzodioxanyl, each optionally substituted with one, two, or three groups independently selected from R^b; each R^a is independently selected from:

- (1) -OR^c,
- (2) -NR^cS(O)_mR^d,
- 25 (3) halogen,
- (4) -S(O)_mR^c,
- (5) -SR^c,
- (6) -S(O)₂OR^c,
- (7) -S(O)_mNR^cR^d,
- 30 (8) -NR^cR^d,
- (9) -O(CR^eR^f)_nNR^cR^d,
- (10) -C(O)R^c,
- (11) -CO₂R^c,
- (12) -CO₂(CR^eR^f)_nCONR^cR^d,

- (13) $-\text{OC}(\text{O})\text{R}^c$,
 (14) $-\text{CN}$,
 (15) $-\text{C}(\text{O})\text{NR}^c\text{R}^d$,
 (16) $-\text{NR}^c\text{C}(\text{O})\text{R}^d$,
 5 (17) $-\text{OC}(\text{O})\text{NR}^c\text{R}^d$,
 (18) $-\text{NR}^c\text{C}(\text{O})\text{OR}^d$,
 (19) $-\text{NR}^c\text{C}(\text{O})\text{NR}^c\text{R}^d$,
 (20) $-\text{CR}^c(\text{N}-\text{OR}^d)$,
 (21) $-\text{CF}_3$,
 10 (22) $-\text{OCF}_3$,
 (23) C_3 -8cycloalkyl, and
 (24) cycloheteroalkyl;
 each R^b is independently selected from:
- (1) C_{1-6} alkyl,
 15 (2) C_{2-6} alkenyl,
 (3) C_{2-6} alkynyl,
 (4) $-\text{OR}^c$,
 (5) $-\text{NR}^c\text{S}(\text{O})_m\text{R}^d$,
 (6) $-\text{NO}_2$,
 20 (7) halogen,
 (8) $-\text{S}(\text{O})_m\text{R}^c$,
 (9) $-\text{SR}^c$,
 (10) $-\text{S}(\text{O})_2\text{OR}^c$,
 (11) $-\text{S}(\text{O})_m\text{NR}^c\text{R}^d$,
 25 (12) $-\text{NR}^c\text{R}^d$,
 (13) $-\text{O}(\text{CR}^e\text{R}^f)_n\text{NR}^c\text{R}^d$,
 (14) $-\text{C}(\text{O})\text{R}^c$,
 (15) $-\text{CO}_2\text{R}^c$,
 (16) $-\text{CO}_2(\text{CR}^e\text{R}^f)_n\text{CONR}^c\text{R}^d$,
 30 (17) $-\text{OC}(\text{O})\text{R}^c$,
 (18) $-\text{CN}$,
 (19) $-\text{C}(\text{O})\text{NR}^c\text{R}^d$,
 (20) $-\text{NR}^c\text{C}(\text{O})\text{R}^d$,
 (21) $-\text{OC}(\text{O})\text{NR}^c\text{R}^d$,

- 5
- (22) $-NR^cC(O)OR^d$,
 - (23) $-NR^cC(O)NR^cR^d$,
 - (24) $-CR^c(N-OR^d)$,
 - (25) $-CF_3$,
 - (26) $-OCF_3$,
 - (27) C_{3-8} cycloalkyl,
 - (28) cycloheteroalkyl, and
 - (29) phenyl;

each R^c and R^d is independently selected from:

- 10
- (1) hydrogen,
 - (2) C_{1-10} alkyl,
 - (3) C_{2-10} alkenyl,
 - (4) C_{2-10} alkynyl,
 - (5) $-NH(C_{1-10}alkyl)$,
 - 15 (6) $-N(C_{1-10}alkyl)_2$,
 - (7) cycloalkyl,
 - (8) cycloalkyl- $C_{1-10}alkyl$;
 - (9) cycloheteroalkyl,
 - (10) cycloheteroalkyl- $C_{1-10}alkyl$;
 - 20 (11) aryl,
 - (12) heteroaryl,
 - (13) aryl- $C_{1-10}alkyl$, and
 - (14) heteroaryl- $C_{1-10}alkyl$, or

25 R^c and R^d together with the atom to which they are attached form a heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N- R^c ,

each R^c and R^d may be unsubstituted or substituted with one to three substituents selected from R^e ;

each R^e and R^f is independently selected from:

- 30
- (1) hydrogen,
 - (2) $C_{1-10}alkyl$,
 - (3) $C_{2-10}alkenyl$,
 - (4) $C_{2-10}alkynyl$,
 - (5) cycloalkyl,

- (6) cycloalkyl-C₁₋₁₀ alkyl,
(7) cycloheteroalkyl,
(8) cycloheteroalkyl-C₁₋₁₀ alkyl,
(9) aryl,
5 (10) heteroaryl,
(11) aryl-C₁₋₁₀ alkyl, and
(12) heteroaryl-C₁₋₁₀ alkyl, or

R^e and R^f together with the carbon to which they are attached form a ring of 5 to 7
members containing 0-2 heteroatoms independently selected from oxygen, sulfur and
10 nitrogen;

m is selected from 1 and 2; and

n is selected from 1, 2, and 3;

for the manufacture of a medicament useful for the treatment of a disease mediated by
the Cannabinoid-1 receptor in a human patient in need of such treatment.

15

27. The use according to Claim 26 wherein the disease mediated by
the Cannabinoid-1 receptor is selected from: psychosis, memory deficit, cognitive
disorders, migraine, neuropathy, neuro-inflammatory disorders, cerebral vascular
accidents, head trauma, anxiety disorders, stress, epilepsy, Parkinson's disease,
20 schizophrenia, substance abuse disorders, constipation, chronic intestinal pseudo-
obstruction, cirrhosis of the liver, asthma, obesity, and other eating disorders
associated with excessive food intake.

28. The use according to Claim 27 wherein the disease mediated by
25 the Cannabinoid-1 receptor is an eating disorder associated with excessive food
intake.

29. The use according to Claim 28, wherein the eating disorder
associated with excessive food intake is selected from obesity, bulimia nervosa, and
30 compulsive eating disorders.

30. The use according to Claim 29 wherein the eating disorder
associated with excessive food intake is obesity.

31. The use of a compound of structural formula I



(I)

or a pharmaceutically acceptable salt thereof, wherein:

5 R¹ is selected from:

- (1) hydrogen,
- (2) C₁₋₄alkyl,
- (3) C₂₋₄alkenyl,
- (4) C₂₋₄alkynyl,
- 10 (5) C₃₋₇cycloalkyl,
- (6) C₃₋₇cycloalkyl-C₁₋₄alkyl,
- (7) cycloheteroalkyl,
- (8) cycloheteroalkyl-C₁₋₄alkyl,
- (9) aryl, and
- 15 (10) heteroaryl;

wherein alkyl, alkenyl, alkynyl, cycloalkyl, and cycloheteroalkyl are optionally substituted with one to four substituents independently selected from R^a, and aryl and heteroaryl are optionally substituted with one to four substituents independently selected from R^b;

20 R² is selected from:

- (1) -OR^c,
- (2) -OC(O)R^c,
- (3) -OC(O)NR^cR^d,
- (4) -SR^c,
- 25 (5) -S(O)_mR^c,
- (6) -SO₂NR^cR^d,
- (7) -NR^cR^d,
- (8) -NR^cC(O)R^d,
- (9) -NR^cSO₂R^d,

- (10) $-\text{NR}^c\text{C}(\text{O})\text{NR}^c\text{R}^d$,
- (11) $-\text{NR}^c\text{C}(\text{O})\text{OR}^d$,
- (12) $-\text{C}(\text{O})\text{OR}^c$, and
- (13) $-\text{C}(\text{O})\text{NR}^c\text{R}^d$;

5 R^3 is selected from:

- (1) $-\text{C}_{1-10}\text{alkyl}$, and
- (2) $-\text{Ar}^2$;

Ar^1 and Ar^2 are independently selected from phenyl, naphthyl, thienyl, furanyl, pyrrolyl, benzothienyl, benzofuranyl, indanyl, indenyl, indolyl, tetrahydronaphthyl, 2,3-dihydrobenzofuranyl, dihydrobenzopyranyl, and 1,4-benzodioxanyl, each optionally substituted with one, two, or three groups independently selected from R^b ; each R^a is independently selected from:

- (1) $-\text{OR}^c$,
- (2) $-\text{NR}^c\text{S}(\text{O})_m\text{R}^d$,
- 15 (3) halogen,
- (4) $-\text{S}(\text{O})_m\text{R}^c$,
- (5) $-\text{SR}^c$,
- (6) $-\text{S}(\text{O})_2\text{OR}^c$,
- (7) $-\text{S}(\text{O})_m\text{NR}^c\text{R}^d$,
- 20 (8) $-\text{NR}^c\text{R}^d$,
- (9) $-\text{O}(\text{CR}^e\text{R}^f)_n\text{NR}^c\text{R}^d$,
- (10) $-\text{C}(\text{O})\text{R}^c$,
- (11) $-\text{CO}_2\text{R}^c$,
- (12) $-\text{CO}_2(\text{CR}^e\text{R}^f)_n\text{CONR}^c\text{R}^d$,
- 25 (13) $-\text{OC}(\text{O})\text{R}^c$,
- (14) $-\text{CN}$,
- (15) $-\text{C}(\text{O})\text{NR}^c\text{R}^d$,
- (16) $-\text{NR}^c\text{C}(\text{O})\text{R}^d$,
- (17) $-\text{OC}(\text{O})\text{NR}^c\text{R}^d$,
- 30 (18) $-\text{NR}^c\text{C}(\text{O})\text{OR}^d$,
- (19) $-\text{NR}^c\text{C}(\text{O})\text{NR}^c\text{R}^d$,
- (20) $-\text{CR}^c(\text{N}-\text{OR}^d)$,
- (21) $-\text{CF}_3$,
- (22) $-\text{OCF}_3$,

(23) C₃-8cycloalkyl, and

(24) cycloheteroalkyl;

each R^b is independently selected from:

- (1) C₁-6alkyl,
- 5 (2) C₂-6alkenyl,
- (3) C₂-6alkynyl,
- (4) -OR^c,
- (5) -NR^cS(O)_mR^d,
- (6) -NO₂,
- 10 (7) halogen,
- (8) -S(O)_mR^c,
- (9) -SR^c,
- (10) -S(O)₂OR^c,
- (11) -S(O)_mNR^cR^d,
- 15 (12) -NR^cR^d,
- (13) -O(CR^eR^f)_nNR^cR^d,
- (14) -C(O)R^c,
- (15) -CO₂R^c,
- (16) -CO₂(CR^eR^f)_nCONR^cR^d,
- 20 (17) -OC(O)R^c,
- (18) -CN,
- (19) -C(O)NR^cR^d,
- (20) -NR^cC(O)R^d,
- (21) -OC(O)NR^cR^d,
- 25 (22) -NR^cC(O)OR^d,
- (23) -NR^cC(O)NR^cR^d,
- (24) -CR^c(N-OR^d),
- (25) -CF₃,
- (26) -OCF₃,
- 30 (27) C₃-8cycloalkyl,
- (28) cycloheteroalkyl, and
- (29) phenyl;

each R^c and R^d is independently selected from:

- (1) hydrogen,

- 5 (2) C₁₋₁₀alkyl,
 (3) C₂₋₁₀ alkenyl,
 (4) C₂₋₁₀alkynyl,
 (5) -NH(C₁₋₁₀alkyl),
 (6) -N(C₁₋₁₀alkyl)₂,
 (7) cycloalkyl,
 (8) cycloalkyl-C₁₋₁₀alkyl;
 (9) cycloheteroalkyl,
 (10) cycloheteroalkyl-C₁₋₁₀ alkyl;
 10 (11) aryl,
 (12) heteroaryl,
 (13) aryl-C₁₋₁₀alkyl, and
 (14) heteroaryl-C₁₋₁₀alkyl, or

15 R^c and R^d together with the atom to which they are attached form a heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-R^c,

each R^c and R^d may be unsubstituted or substituted with one to three substituents selected from R^e;

each R^e and R^f is independently selected from:

- 20 (1) hydrogen,
 (2) C₁₋₁₀alkyl,
 (3) C₂₋₁₀ alkenyl,
 (4) C₂₋₁₀alkynyl,
 (5) cycloalkyl,
 25 (6) cycloalkyl-C₁₋₁₀ alkyl,
 (7) cycloheteroalkyl,
 (8) cycloheteroalkyl-C₁₋₁₀ alkyl,
 (9) aryl,
 (10) heteroaryl,
 30 (11) aryl-C₁₋₁₀ alkyl, and
 (12) heteroaryl-C₁₋₁₀ alkyl, or

R^e and R^f together with the carbon to which they are attached form a ring of 5 to 7 members containing 0-2 heteroatoms independently selected from oxygen, sulfur and nitrogen;

m is selected from 1 and 2; and

n is selected from 1, 2, and 3;

for the manufacture of a medicament for the prevention of obesity in a person at risk therefor.

5